Illustrative Teaching Case

More to Atherosclerosis Than Stenosis
Symptomatic Carotid Artery With Intraplaque Hemorrhage

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Case Description
A 66-year-old man presented with left facial weakness on awakening. He had cerebrovascular risk factors, including HIV, hypertension, and hyperlipidemia. When the facial weakness did not resolve after a few days, he presented to a local hospital. A brain magnetic resonance imaging scan, including an axial diffusion-weighted imaging sequence, demonstrated an ischemic stroke in the face representation area of the right precentral gyrus. Transthoracic echocardiography, carotid ultrasound, and cardiac telemetry were unrevealing. He was prescribed dual antiplatelet therapy and a statin. He was referred to a vascular neurologist at our tertiary care center. After seeing the vascular neurologist, a noncontrast magnetic resonance angiogram (MRA) of the head and neck was obtained: 3-dimensional (3D) time-of-flight (TOF) imaging demonstrated ≤50% stenosis of the carotid bulbs bilaterally (40%–50% bilaterally by NASCET criteria [North American Symptomatic Carotid Endarterectomy Trial]). On these T1-weighted images and on a fat-suppressed axial T1 sequence, there were focal, crescentic, subintimal hyperintense signals at the bifurcations bilaterally (Figure 1). The findings were highly suggestive of intraplaque hemorrhage. However, given the modest degree of stenosis and an incomplete etiologic investigation, the right carotid artery was not yet considered definitively symptomatic. He then underwent 30 days of extended cardiac rhythm monitoring to investigate occult arrhythmias as a potential source of the presumed embolic stroke. The facial weakness completely resolved.

Two months later, he developed recurrent left facial weakness accompanied by new left arm weakness and dysarthria. When he presented to the local hospital, his National Institutes of Health Stroke Scale (NIHSS) was 5. He was not treated with intravenous tPA (tissue-type plasminogen activator) because of a delay in presentation. A carotid ultrasound was performed to better visualize possible carotid endarterectomy. After careful deliberation between neurology, vascular surgery, and neuroradiology, a carotid endarterectomy was performed. Intraoperatively, the vascular lesion was identified as a round, dark red protrusion on the outside of the right proximal internal carotid artery (ICA). The resected lesion was found to be the source of emboli. Vascular surgery was consulted to evaluate for possible carotid endarterectomy. Despite only demonstrating a modest degree of internal carotid artery stenosis, the right carotid lesion was thought to be the source of emboli. Vascular surgery was consulted to evaluate for possible carotid endarterectomy. After careful deliberation between neurology, vascular surgery, and neuroradiology, a carotid endarterectomy was performed. Intraoperatively, the vascular lesion was identified as a round, dark red protrusion on the outside of the right proximal internal carotid artery (ICA). The resected lesion was found to be an ulcerated, ruptured, hemorrhagic plaque (Figure 3).

Despite not being identified as an embolic stroke, the patient was discharged to a rehabilitation facility on antiplatelet and high-dose statin therapy.

Discussion
We present a patient with an embolic ischemic stroke and early stroke recurrence in the setting of extracranial large artery atherosclerosis with high-risk morphological features but <50% stenosis. Current American Heart Association/American Stroke Association (AHA/ASA) guidelines only address the degree of arterial narrowing (% stenosis) when recommending the use of carotid revascularization procedures for secondary...
stroke prevention. This guideline is largely informed by the NASCET, VACS (Veterans Affairs Cooperative Study), and ECST (European Carotid Surgery Trial) trials that found benefit for carotid endarterectomy in patients with a symptomatic carotid stenosis of ≥70%. The most recent AHA/ASA guideline advises against revascularization procedures in patients with <50% extracranial ICA stenosis. In NASCET, the arm of the trial assessing efficacy in patients with symptomatic carotid stenosis of 30% to 69% did not demonstrate clear benefit. This group was later subdivided, showing modest benefit for surgery with 50% to 69% stenosis. These guidelines and clinical trials do not account for plaque morphology that may predict a high risk of early stroke recurrence as demonstrated by our patient.

Given this patient’s HIV status, one may wonder if this disease played a role in his atherosclerotic plaque morphology. Although there is evidence from previous studies to indicate an association between HIV and large artery atherosclerosis in patients with ischemic stroke, a more recent study suggests

Figure 1. Initial presenting magnetic resonance imaging and magnetic resonance angiogram (MRA). A, Axial diffusion-weighted imaging demonstrates a small acute infarct in the right precentral gyrus. B, Axial noncontrast MRA raw image of the neck demonstrates narrowing of the carotid bulbs with peripheral hyperintense signals (arrows, indicating intrinsic T1 hyperintensities) consistent with intraplaque hemorrhage. C, Three-dimensional MRA maximal intensity projection shows the narrowing of the carotid bulb and the adjacent intraplaque hemorrhage (arrow). D, Axial T1 fat-suppressed images corroborates the intrinsic T1 hyperintensity in the vessel wall (arrows) seen in B.

Figure 2. Follow-up magnetic resonance imaging and magnetic resonance angiogram (MRA). A, Axial diffusion-weighted imaging demonstrates numerous new acute infarcts throughout the right middle cerebral artery territory. B, Raw images from the 2-dimensional time-of-flight MRA show narrowing of the carotid bulbs, but the intraplaque hemorrhage is difficult to identify. C, Raw image from the postcontrast subtraction of the MRA neck showing narrowing of the vessel; note that the intraplaque hemorrhage is not well seen. D, Noncontrast raw image from the MRA neck used for subtraction demonstrates the peripheral T1 hyperintensity (arrow), which is likely similar to the initial MRA, although it is not as well seen given differences in technique.
that the main factors that independently increase risk of stroke for people with HIV are immunosuppression (CD4+ cell count <500/µL) and viremia (HIV RNA >500/mL), after adjusting for other vascular risk factors. Our patient was immunocompetent with an undetectable viral count, making HIV a less likely contributor in his case.5

Because of its noninvasive nature and low cost, ultrasonography remains a widely used modality for the evaluation of carotid stenosis. Recent studies have looked at advances in ultrasound technique to assess plaque morphology as a predictor of plaque stability, independent of the degree of stenosis. In a study using ultrasound digital imaging analysis software to assess plaque echodensity and texture, echoluency and homogeneity were associated with unstable histological phenotypes.6 These techniques have largely been limited to research settings and are not used in routine clinical practice.

Computed tomography angiography and MRA can identify atherosclerotic lesions in the carotid arteries with high levels of accuracy, sensitivity, and specificity. Computed tomography angiography can discriminate between lipid components, fibrous components, and the calcium present in atheromas.7 T1-weighted images on magnetic resonance imaging can help to identify subintimal hemorrhage. Accordingly, both modalities can be helpful in assessing clinically relevant morphological features of extracranial carotid plaques.8 Carotid intraplaque hemorrhage may be an independent risk factor for recurrent cerebral ischemia and may identify those that would benefit from early surgical intervention.9

However, as demonstrated in this case, the sensitivity and specificity can vary depending on the imaging sequence (and the scanner) used. A 3D TOF sequence will be far superior to a 2D TOF sequence. Axial T1 fat-suppressed images can be complementary on all of these scanners. Moreover, the findings on a postcontrast MRA neck sequence are only apparent if the noncontrast images used for subtraction of the MRA are reviewed. Thus, it is important to be aware of local variations in practice, and how intraplaque hemorrhage will appear on the sequence used in the carotid evaluation.

Patients may require advanced or multimodal imaging for optimal assessment of their atherosclerotic plaques. Our patient presented with recurrent stroke secondary to symptomatic carotid disease that did not meet criteria for carotid endarterectomy following current guidelines. Ultrasonography did not detect the high-risk morphological features of the ICA plaque in this patient. Combining the intraplaque hemorrhage on MRA and the clinical history, we referred the patient for surgical intervention based on clinical judgment. This case demonstrates the importance of considering surgical intervention when plaque morphology is suggestive of a high-risk extracranial ICA lesion as the source of emboli. Plaques can be considered embolically significant even though hemodynamically they are not.

TAKE-HOME POINTS

- Although clinical trials to date have not addressed atherosclerotic plaque morphology, this should be considered when determining the source of cerebral or retinal emboli (especially in the setting of failing medical therapy) and when selecting patients for revascularization procedures.
- Computed tomography angiography and magnetic resonance angiogram are essential, and potentially complementary, imaging modalities for assessing the extracranial and intracranial vasculature for culprit lesions. Variations in magnetic resonance angiogram neck technique need to be understood to be able to maximize diagnosis of potentially vulnerable plaques. Carotid ultrasonography is less sensitive for detecting clinically relevant morphological plaque features.

Disclosures

None.

References


Figure 3. Surgical specimen of the right proximal internal carotid artery (ICA) from carotid endarterectomy. A, Hemorrhagic plaque on external view of the ICA. B, Internal view of ICA demonstrating ruptured hemorrhagic plaque.


**KEY WORDS:** atherosclerosis ▼ carotid stenosis ▼ dysarthria ▼ hypertension ▼ stroke
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Stroke. 2017;48:e104-e107; originally published online March 14, 2017; doi: 10.1161/STROKEAHA.117.016923

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